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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,240	03/23/2005	Stefan Wildt	GFI-102	3290

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,240	WILDT ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-12,14,15,17 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-12,14,15,17 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/2/07,12/19/07,8/21/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of June 19, 2007 on June 29, 2009. Claims 1, 6 are amended. Claims 4, 5, 13, 16, 18-58, 60-65 are cancelled.

Claims 1-3, 6-12, 14, 15, 17, 59, drawn to a method for producing a recombinant glycoprotein is under consideration. As a reminder, per the species election by Applicant, November 11, 2006, Applicant elected, "alpha-1, 2 mannosidase" (claim 7), "dolichyl-P-Man: Man5GlcNac2-PP-dolichyl alpha-1,3, mannosyltransferase" (i.e., Alg3) (claims 8, 9), "GlcNac" (claims 12-15), and "Pichia pastoris" (claim 17).

Specification

Applicant's arguments, see response, filed December 22, 2008, with respect to the filing of sequences in computer readable format (CRF) and on paper, amendments to the specification indicating SEQ ID NOs., and a statement indicating that the CRF and the paper sequences are the same have been fully considered and are persuasive. The objection of specification has been withdrawn.

Information Disclosure Statement

Applicant filed Information Disclosure Statements (IDSes) on August 2, 2009, December 19, 2007, and August 21, 2009. The IDSes has been considered.

Withdrawn Objection/Rejection

Claim Objection

Applicant's arguments, see page 11 of Applicant's response, filed June 29, 2009, with respect to the objection of claim 6 have been fully considered and are persuasive. Applicant indicates that claim 6 has been amended to delete "glycosyltransferase." The issue regarding this objection is withdrawn. With regard to the objection of claim 46, Applicant has cancelled the claim. As such, the objection as it applies to this issue is withdrawn.

Double Patenting

Applicant's arguments, see page 11 of Applicant's response, filed June 29, 2009, with respect to the rejection of claims 1-4, 6, 7, 10, 11, 14-17 on the grounds of nonstatutory obviousness-type double patenting over US Patent 7,029,872 ('872) have been fully considered and are persuasive. Applicant indicates that the inventions of claims '872 and the instant application are distinct because the '872 claims are directed to modifications when the oligosaccharide is protein-linked; the instant claims are drawn to modifications when the oligosaccharide is lipid-linked. The rejection of claims 1-4, 6, 7, 10, 11, 14-17 has been withdrawn.

Applicant's arguments, see page 12 of Applicant's response, filed June 29, 2009, with respect to the rejection of claims 1-4, 8-11, 14-17, 59 on the grounds of nonstatutory obviousness-type double patenting over co-pending

Application 10/371,877 ('877) have been fully considered and are persuasive. Applicant indicates that the inventions of claims '877 and the instant application are distinct because the '877 claims are directed to modifications when the oligosaccharide is protein-linked; the instant claims are drawn to modifications when the oligosaccharide is lipid-linked. The rejection of claims 1-4, 8-11, 14-17, 59 has been withdrawn.

Applicant's arguments, see page 13 of Applicant's response, filed June 29, 2009, with respect to the rejection of claim 46 on the grounds of nonstatutory obviousness-type double patenting over co-pending Application 11/187,066 ('066) have been fully considered and are persuasive. Applicant indicates that claim 46 is cancelled. As such, the rejection of claim 46 is withdrawn.

35 USC § 112, 1st parag.

Applicant's arguments, see page 13 of Applicant's response, filed June 29, 2009, with respect to the rejection of claims 1-4, 6-12, 14-17, 46, 59 have been fully considered. Upon further consideration, the rejection of the claims have been withdrawn as the art teaches that it is common for artisans to express transgenes comprising sequences that encode glycosylation enzymes and to disrupt endogenous glycosylation enzyme genes in microorganisms such as yeast. As such, the rejection as it applies to these issues is withdrawn.

35 USC § 112, 2nd parag.

Applicant's arguments, see pages 13-14 of Applicant's response, filed June 29, 2009, with respect to the rejection of claim 4 have been fully considered and are persuasive. Applicant indicates that claim 4 is cancelled. As such, the rejection of claim 4 is withdrawn.

35 USC § 102

Applicant's arguments, see page 14 of Applicant's response, filed June 29, 2009, with respect to the rejection of claims 1-4, 6, 7, 10, 11, 14-17, 46 as being anticipated by Gerngross '872 have been fully considered and are persuasive. Applicant indicates that Gerngross '872 is directed to diminishing or depleting enzymes that transfer a sugar to the 1,6 arm of a protein linked arm and not a lipid-linked arm. The rejection of claims 1-3, 6, 7, 10, 11, 14, 15, 17 has been withdrawn. The rejection of claims 4, 16, 46 is withdrawn as the claims are cancelled.

Applicant's arguments, see pages 14-15 of Applicant's response, filed June 29, 2009, with respect to the rejection of claims 1, 4, 10-12, 15-17, 46 as being anticipated by Chiba et al., 1998 have been fully considered and are persuasive. Chiba et al. do not teach"diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure." The rejection of claims 1, 10-12, 15, 17 has been withdrawn. It is noted that the rejection of claims 4, 16, 46 is withdrawn as the claims are cancelled.

Applicant's arguments, see page 15 of Applicant's response, filed June 29, 2009, with respect to the rejection of claim 46, as being anticipated by Kornfeld, 1983, Wagner et al., 1996, and Velasco et al., 1993 have been fully considered and are persuasive. Applicant indicates that claim 46 is cancelled. The rejection of claim 46 has been withdrawn.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-12, 14, 15,17, 59 are newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The final Written Description Examination guidelines that were published on January 5, 2001 (66 FR 1099; available at http://www.uspto.gov/web/menu/current.html#register).

The written description requirement for a claimed genus is satisfied by sufficient description of a representative number of species by actual reduction to practice and by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties by functional characteristics coupled

with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicant were in possession of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

While the specification and the art provides adequate written description for Alg12 being an enzyme that transfers a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure, the specification fails to adequately describe other enzymes that have this biological activity. Note that claim 1 is drawn to "one or more enzymes" that have this activity. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646

(1998). In the instant case, while the art, Burda et al., 1999, Biochimica et Biophysica Act, 1426: 239-257, Figures 1 and 2, and specification (Figure 1) teach that Alg12 catalyzes the addition of an alpha 1,6 linked mannose on lipid-linked oligosaccharides, the specification provides no guidance for other enzymes with this activity. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only Alg12 meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8, 9 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Alg3 (dolichyl-P-Man:Man5GlcNac2, PP-dolichyl alpha-1,3 mannosyltransferase), in claims 8 and 9, is not an enzyme that transfers a sugar residue to the 1,6 arm of an oligosaccharide. It transfers a sugar to the 1,3 arm of the sugar.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 6, 7, 10-12, 14, 15, 17, 59 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Goss et al., 1995, Clinical Cancer Research, 1: 935-944, Yoshida WO 00/34490, published June 15, 2000, Gemmill et al., 1999, Biochimica et Biophysica Acta, 1426: 227-237, Burda et al., 1999a, Biochimica et Biophysica Acta, 1426: 239-257, Karaoglu et al., 2001, Biochemistry, 40: 12193-12206, Burda et al., 1999b, Glycobiology, 9: 617-625, Tremblay et al., 1998, Glycobiology, 8: 585-595, Sarkar et al., 1991, PNAS, USA, 88: 234-238, Moremen et al., 1991, The Journal of Cell Biology, 115: 1521-1534.

At the time of filing, Goss et al. teach that GlcNAcMan3GlcNAc2-N is a substrate for GlcNAc-Ts (i.e. GlcNAc-T-II, -IV, -V), wherein each enzyme substitutes a distinct position on the trimannose core to initiate branches. Cancer cells commonly shown increased beta1-6-N-acetylglucosamine (GlcNAc-)

branching at the trimannosyl core of N-linked carbohydrates (Goss et al., page 935, 2nd col., 1st parag. under Carbohydrate Processing and Malignancy).

While Goss et al. teach that GlcNAcMan3GlcNAc2-N is a useful substrate used to study changes in glycosylation patterns as seen in cancer cells, they do not teach how to obtain GlcNAcMan3GlcNAc2-N.

At the time of filing, the art teaches that artisans were interested in using other organisms to make proteins that have human-type glycosylation (Yoshida, abstract). In addition to yeast, taught by Yoshida, other organisms can be used as well as Gemmill et al. teach that yeast and most higher eukaryotes have an evolutionarily conserved N-linked oligosaccharide biosynthetic pathway (Gemmill et al., abstract). As such, it would have been as likely for an artisan to use a plant or a yeast to make proteins that have glycosylation structures heterologous to the host making the recombinant protein. With regard to teaching lipid-linked oligosaccharides, Burda et al., 1999a, Figure 2 teach lipid-linked oligosaccharide synthesis and enzymes to add or remove components on the oligosaccharide were known. In addition to this, it was known that lipid-linked intermediates can be transferred to asparagine residues on peptides by oligosaccharyltransferase, although there is preference for the fully assembled dolichol-linked oligosaccharide (Karaoglu et al., abstract). Given Karaoglu et al.'s teaching, an artisan can take any oligosaccharide intermediate bound to lipid and transfer it to an asparagine in a protein. With regard to yeast comprising a disruption in the enzyme that transfers a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide, Burda et al. 1999b teach that the Alg12 mutant yeast has this

defect. An artisan could take the Alg12 mutant yeast and obtain Man6GlcNAc2. With regard to processing Man6GlcNAc2 to GlcNAcMan3GlcNAc2, Yoshida teaches that Man6GlcNAc2 can be treated with Mannosidase I (Man I) to remove the alpha-1,2 linked sugars and teaches that Man4GlcNAc2 interacts with N-acetylglucosaminyl transferase I (GlcNAc I) to produce GlcNAcMan4NAc2. Mannosidase II (Man II) then removes the alpha-1,3 linked mannose from GlcNAcMan4GlcNAc2 to yield GlcNAcMan3GlcNac2 (Yoshida, page 3). With regard to the nucleic acid sequence of mannosidase I, Tremblay et al., 1998 teach the sequence of alpha-1,2 mannosidase IB, which can remove 4 alpha-1,2 mannose residues. With regard to GlcNacI, Sarkar et al., teach the nucleic acid sequence (Sarkar et al., Figure 4), and with regard to mannosidase II, Moremen et al. teach the sequence.

All of the component parts are taught in Goss et al., Yoshida, Gemmill et al., Burda et al., 1999a, Karaoglu et al., Burda et al., 1999b, Trembaly et al., Sarkar et al., and Moremen et al. The only difference is the combination of the "old elements" into a single method of producing a recombinant protein in a unicellular or filamentous fungus, wherein the recombinant protein has an N-glycans GlcNAcMan3GlcNAc2 attached to it.

It would have been obvious for an ordinary artisan to take mutant yeast that synthesize oligosaccharides of a desired structure and to modify the oligosaccharide to GlcNAcMan3GlcNAc2 such that an artisan would arrive at a glycoprotein that can be modified for cancer studies. With regard to the particular limitations of the claims, Burda et al., 1996b teach that yeast with a

mutation in transferring sugar to the 1,6 arm of a lipid-linked oligosaccharide was known (Alg12) and that those oligosaccharides can be transferred to an asparagine residue on a protein (Karaoglu et al.). Enzymes (and their coding sequences) that remove sugars and add GlcNAc were also known (Yoshida, Tremblay et al., Sarkar et al, and Moremen et al.).

Thus, the claims are obvious.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Joanne Hama/
Primary Examiner
Art Unit 1632